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| MERCK AND CO., INC | | WEHBE, ANNE MARIE SABRINA | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

ATTACHMENT TO ADVISORY ACTION

11. CONT. The rejection of claims 1-12, and 21-26 under 35 U.S.C. 103(a) as being unpatentable over WO 96/04932 (1996), hereafter referred to as Balasubramanian et al., in view of WO 97/25072 (1997), hereafter referred to as Engler et al., is maintained over claims 1-13 and 21-26. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant reiterates their argument that Engler et al. teaches away from combining a cationic surfactant with a high molecular weight block copolymer such as CRL-1005 by showing that neither benzalkonium chloride nor cetylpyridium enhanced gene transfer. In their opinion the data in Example 5 of Engler is not conclusive since no negative control data was presented, and accordingly, the applicant concludes that skilled artisan viewing the Engler data would not find that cationic detergents and some of the nonionic detergents had any effect on gene transfer.

In response, it is first noted that the claims under examination are product claims, not method claims for enhancing gene transfer. Second, as discussed in the previous office action, Engler was cited to supplement Balasubramanian et al. by teaching that cationic detergents, a class of surfactants, can be included in a composition for gene delivery resulting in the delivery of nucleic acids to cells (Engler et al., pages 4-5, and 20-21). In the working examples on pages 14-15, Engler et al. demonstrates that while some surfactants improve gene transfer more than others, Engler et al. clearly shows positive gene transfer using DNA in the form of recombinant adenoviral vector and cationic surfactants. Applicant's contention that the lack of negative control invalidates these results is not agreed. Neither is it agreed that the use of a "+" in the result column for gene transfer and expression would be interpreted by a skilled artisan as background staining. The specification indicates that the "+" represents minimal staining, not background or negative staining. While it may be agreed that the "<+" staining observed for the cationic detergent benzalkonium chloride might be considered a negative result, the "+" staining observed using the cationic detergent cetylpyridium appears to indicate gene transfer and expression absent any concrete evidence to the contrary. The fact that some other detergents results in "+++" staining also does not teach away from the use of a cationic detergent- "[a]

known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Further, the office maintains that Engler et al. makes the clear statement that cationic detergents/surfactants can be used to enhance gene delivery. The fact that Engler lists more than reagent capable of having this effect does not "teach away" from the inclusion of cationic detergents in a gene delivery composition. As such, applicant's argument that Engler et al. teaches away from using cationic detergents is not found persuasive.

Further, as indicated above, the instant claims are product claims, not methods claim for using the product to enhance gene delivery or improve expression of a transgene. The claimed product elements are obviated by the combined teachings of Balasubramanian et al., who teaches the combination of polynucleotide vaccines, a nonionic surfactant, and an adjuvant comprising a high molecular weight nonionic polyoxyethylene/ polyoxypropylene block copolymers of the general formula HO(C₂H₄O)_a(C₃H₆O)_b(C₂H₄O)_aH, such as CRL-1005, and Engler et al. who teaches that cationic surfactants can be added to DNA delivery systems resulting in gene transfer. Further, based on the demonstration by Engler et al. that a formulation comprising a recombinant adenoviral vector and a cationic surfactant such as cetylpyridium can be delivered to cells resulting in detectable gene expression, the skilled artisan would have predicted that a combination as claimed, comprising an adjuvant comprising a high molecular weight nonionic polyoxyethylene/ polyoxypropylene block copolymers of the general formula HO(C₂H₄O)_a(C₃H₆O)_b(C₂H₄O)_aH, such as CRL-1005, a polynucleotide DNA vaccine, a nonionic surfactant, and a cationic surfactant would be capable of being delivered to cells with the result of gene expression. A demonstration of "enhanced" gene delivery is not required to obviate the claimed compositions as this property is not a claimed limitation.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the new technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology

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center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

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Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

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